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N-[4-(Pyrrolidin-1-ylcarbonylmethoxy)phenyl]-acetamide

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Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.003 Å
Disorder in main residue
R factor = 0.059
wR factor = 0.183
Data-to-parameter ratio = 14.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title compound, $C_{14}H_{18}N_2O_3$, is a potential anti-amnesic agent. The pyrrolidine ring is disordered and both major and minor components adopt an envelope conformation. In the solid state, symmetry-related molecules are linked by intermolecular N—H···O hydrogen bonds, forming chains with a C(10) graph-set motif. Intermolecular C—H···O interactions are also observed.

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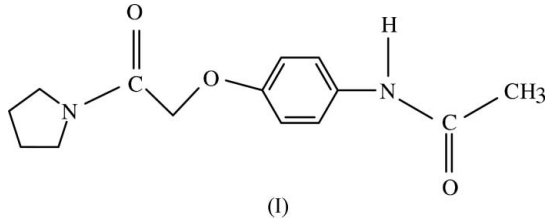
Comment

The conformations of molecules with anti-amnesic activity have attracted considerable interest (Amato *et al.*, 1991). The crystal structures of several new classes of anti-amnesic agents have been reported from our laboratory (Thamotharan, Parthasarathi, Gupta *et al.*, 2003*a*,*b*, and references therein; Thamotharan, Parthasarathi, Malik *et al.*, 2003*a*,*b*, and references therein). As a continuation of our studies, the X-ray crystal structure determination of the title compound, (I), was undertaken.



(I)

A view of the molecule of (I) with the atom-numbering scheme is shown in Fig. 1. One of the C atoms in the pyrrolidine ring is disordered over two sites (C10 and C10′) with occupancy factors of 0.646 (15) and 0.354 (15). An envelope

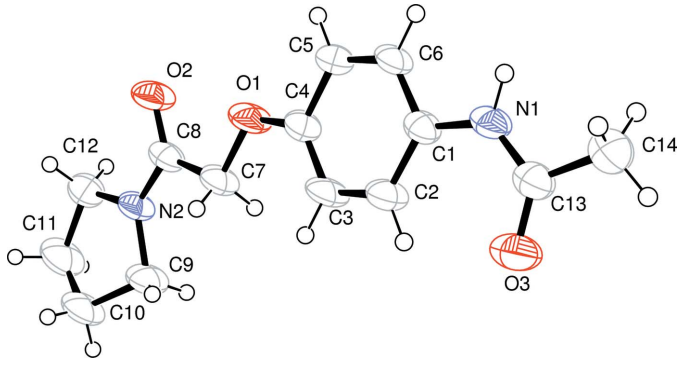


Figure 1
View of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are shown by circles of arbitrary radii. For clarity, only the major conformation of the disordered pyrrolidine ring is shown.

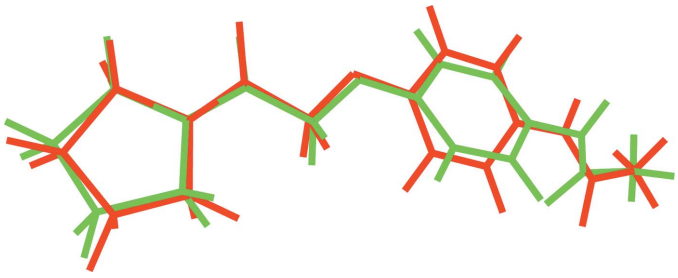


Figure 2
Superimposed fit of the crystal structure of the major conformation (red) of (I) and its energy minimized counterpart (green).

conformation is observed for the major component of the disordered pyrrolidine ring, with puckering parameters Q = 0.284 (6) Å and φ = 67.1 (8)° for the atom sequence N2—C9—C10—C11—C12, with atom C10 in the flap position (Cremer & Pople, 1975). The minor component defined by the atom sequence N2—C9—C10′—C11—C12 also exhibits an envelope conformation with atom C10′ in the flap position [puckering parameters Q = 0.227 (9) Å and φ = 260.8 (11)°].

The angle C1—N1—C13 [130.06 (18)°] is comparable to the corresponding angle in three related structures, *viz.* *N*-[4-(4-methylpiperazin-1-ylsulfonyl)phenyl]acetamide hydrate, (II) [128.43 (19)°; Guo, 2004], *N*-(4-amino-2-methoxyphenyl)acetamide, (III) [129.78 (17)°; Robin *et al.*, 2002] and *N*-[4-(acetyloxy)phenyl]acetamide, (IV) [128.8 (2)°; Caira *et al.*, 1999]. The significantly large value of the angle C1—N1—C13, when compared to the normal value of 120°, may be due to an intramolecular short contact between the atoms O3 and H2 (2.37 Å), which is less than the sum of their van der Waals radii (2.60 Å). Similar short contacts are observed between the corresponding atoms in (II) (2.30 Å) and (III) (2.38 Å). This might have been due to the crystal packing effect. In order to understand the packing effect on the molecules, energy minimization was carried out on the isolated molecule using the WinMopac 7.21 program (Shchepin & Litvinov, 1998). A least-squares fit of the energy minimized molecule with the major component of (I) gives an r.m.s. deviation of 0.579 Å (Fig. 2). Thus, the conformations of the molecule in the crystal and the free molecule are slightly different. In the energy minimized molecule, the rotation about the N—C bond has obviously reduced the strain that was observed in the molecules of the crystal, which is evident from the O3—H2 distance of 3.2 Å and the C1—N1—C13 angle of 128.42°.

The central O1/C7/C8/O2 fragment is planar, with a maximum deviation of 0.014 (1) Å for atom C8. Atoms N1/C13/O3/C14 of the acetamide residue lie in a plane with a maximum deviation of 0.005 (2) Å for atom C13. The dihedral angle between the least-squares plane of the plane of the central fragment and the benzene ring is 4.4 (2)°. The dihedral angle between the acetamide residue and the benzene ring is 4.9 (2)°. This indicates that the central fragment and acetamide residue are almost coplanar with the benzene ring.

A least-squares fit of the phenyl acetamide moiety of (I) with that in (II), (III) and (IV) gives r.m.s. deviations of 2.829, 2.735 and 2.930 Å, respectively. This shows that the conformations of the phenylacetamide moiety are different due to the different types of substitutions in effect at the *para* position of the benzenel ring.

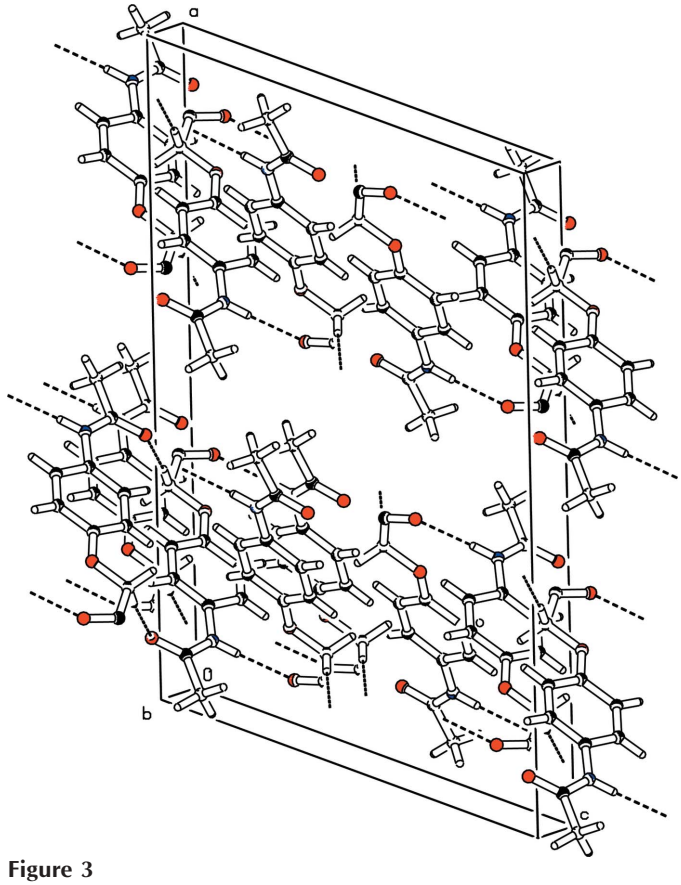


Figure 3
Part of the crystal structure of (I), showing N—H···O interactions. The intermolecular hydrogen bonds are shown by dashed lines.

In (I), atom N1 forms an intermolecular hydrogen bond with carbonyl atom O2 of a symmetry-related molecule (Table 2). This interaction links the molecules into a continuous chain, which runs parallel to the *c* axis and has a graph-set motif of $C(10)$ (Bernstein *et al.*, 1995) (Fig. 3). Atom C7 acts as a donor in a strong intermolecular C—H···O interaction *via* H7*A* with carbonyl atom O3 of a symmetry-related molecule (Table 2) (Desiraju, 1997).

Experimental

Excess of pyrrolidine was addded to methyl 2-(4-acetamidophenoxy)acetate (1.0 g, 4.48 mmol) and was stirred with a magnetic stirrer. Crushed ice was added and the white solid obtained was crystallized from acetone (yield 642.4 mg, 54.67%; m.p. 445–447 K).

Crystal data

$C_{14}H_{18}N_2O_3$
M_r = 262.30
Monoclinic, $C2/c$
a = 21.08 (2) Å
b = 10.927 (11) Å
c = 12.767 (9) Å
β = 111.12 (2)°
V = 2743 (4) Å^3
Z = 8
D_x = 1.270 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 745 reflections
θ = 2.3–28.3°
μ = 0.09 mm^{-1}
T = 298 (2) K
Block, colourless
0.4 × 0.2 × 0.1 mm

Data collection

Bruker SMART CCD 1K diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.965, T_{max} = 1.000
14787 measured reflections
2787 independent reflections
1837 reflections with $I > 2\sigma(I)$
R_{int} = 0.061
θ_{max} = 26.5°
$h = -26 \rightarrow 24$
$k = -13 \rightarrow 13$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.183
S = 1.04
2787 reflections
187 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1129P)^2 + 0.0652]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.21 e Å^{-3}

Table 1
Selected torsion angles (°).

C13—N1—C1—C6	179.5 (2)	C4—O1—C7—C8	178.33 (17)
C13—N1—C1—C2	−2.7 (3)	O1—C7—C8—O2	−3.0 (3)
C7—O1—C4—C3	−1.7 (3)	C1—N1—C13—O3	−0.8 (4)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^{i}	0.87 (3)	2.03 (3)	2.900 (3)	176 (2)
C2—H2···O3	0.93	2.37	2.958 (4)	121
C7—H7A···O3^{ii}	0.97	2.54	3.501 (4)	174

Symmetry codes: (i) $-x+\frac{1}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+\frac{1}{2}, -y+\frac{5}{2}, -z$.

One of the C atoms in the pyrrolidine ring is disordered over two sites, C10 and C10′, with occupancy factors of 0.646 (15) and 0.354 (15), respectively. Atom H1 was located from a difference Fourier map and refined freely. All other H atoms were placed in geometrically idealized positions (C—H = 0.93–0.97 Å) and constrained to ride on their parent atoms, with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for others.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP3* (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PARST* (Nardelli, 1995).

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